Studies of Acid Aerosols in Six Cities and in a New Multi-City Investigation: Design Issues

by Frank E. Speizer*

Techniques for measuring acid aerosols in the ambient environment have been developed only recently. As part of the on-going Harvard Study on the Health Effects of Sulfur Dioxide and Respirable Particulates, we have developed monitoring equipment for acidic particles that can be used in multiple field settings. Preliminary data suggest that these strong acid aerosol measurements may correlate with respiratory symptoms more closely than similar measurements of particulate matter less than 15 µm in size. These results have led to the beginning of a U.S.-Canadian cooperative study to assess the chronic effects of acid aerosols on the health of North American children. Communities are being selected on the basis of anticipated levels of H_2SO_4 in ambient air along with predicted levels of ozone and nitrates. Each community will undergo a 1-year period of every other day, 24-hr monitoring with newly developed monitoring equipment that will allow for quantification of H^+ ion concentrations, as well as for specific measures of ozone and acid fractions. At the end of the 1-year period, while measurements are still being made, approximately 600 children aged 7 to 11 in each of up to 24 communities will be assessed with standardized questionnaires completed by parents, and pulmonary function will be measured in the children while in school. By estimating chronic exposure from the year-long measurement of acid aerosols and consideration of specific criteria for selecting communities to study, we hope to minimize potential confounding to allow us to assess the chronic impact of strong acid in the atmosphere on the respiratory health of these children.

Introduction

The public and scientific debate over acid rain and its precursors has focused on the ecological effects and secondary health effects related to mobilization of toxic metals. Far less concern has been shown for direct human health effects, either acute or chronic, due to acid aerosols (1). Oxidation of primary pollutants (sulfur and nitrogen oxides) to acidic gases and particles is clearly identified as the main source of these agents. Whether existing control strategies could be implemented without devastating economic implications is not clear. How successful partial controls would be is unknown.

There are remarkably few data on the health impact of either current or past exposures to acidic air pollution. Clearly, large scale air pollution disasters in the middle of this century involved acid aerosols, as well as primary pollutants such as sulfur dioxide (SO_2) and smoke. From what has subsequently been learned about the acute effects of SO_2, it is very likely that the

offending agent in those episodes was the particulate matter. The acidity of those particles could have played a major role, particularly in individuals with compromised cardiopulmonary systems.

Fortunately, it is not likely that levels of exposure resulting in the episodes identified from the 1940s to the 1960s will occur again in North America. However, it is unknown whether less severe daily or cumulative exposures to acid aerosols and gases can affect respiratory symptoms either by themselves or in conjunction with other pollutants. Animal and clinical studies in relatively small groups of subjects suggest the possibility of such adverse effects at sulfuric acid concentrations of 100 $\mu g/m^3$ (2–5). Whether entire populations or only sensitive groups are affected is not known.

Although epidemiologic studies suggest that groups of free-living individuals may be affected by air pollution in general, there are no population-based studies that have directly measured acid aerosol exposure and response. Part of the problem has been the lack of an operational monitoring system for measurement of gaseous and aerosol acidity in ambient air. Mass of size-fractionated particles (PM_{10} or $PM_{2.5}$), SO_2 or

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nitrogen dioxide (NO_2), and total particulate sulfate (TSO_4), coupled with recent measures of acidic rain water, have been presumed to represent surrogates for acid aerosols, in the absence of a suitable method for direct measurement of airborne acidity.

Although natural sources of these pollutants exist, their primary origin in the eastern half of North America is sulfur and nitrogen oxides released into the atmosphere from point sources and oxidized during airborne transport to sulfuric and nitric acids. Nitrogen oxides primarily come from transportation and electric utilities. Sulfur oxides result from industrial processes and coal- and oil-fired power plants.

Assumed emission patterns, climatic wind patterns (6), and the distribution of acid precipitation (7) suggest that elevated acid aerosol concentrations would be expected from the upper Ohio Valley region on into Southern Ontario. These findings led Bates and Sizto (8,9) to evaluate hospital admission rates for respiratory conditions in Southern Ontario. No direct acid aerosol measurements were made in these studies.

In another study of respiratory symptoms in a population of 5500 women from a rural area of Western Pennsylvania, respiratory symptoms were associated with levels of SO_2 (10). Again, no direct measures of acid were available; however, air mass trajectories for this rural setting were suggestive of transport of acid aerosols into this region.

In this report we present one of the health findings in children from the Harvard Study of Air Pollution and Health (Six-Cities Study) and suggest how that result might be modified by the available acid data. We will then discuss the direction of some of the analyses currently underway to assess the effect of acid aerosols on daily symptoms. We will spend the bulk of the discussion on the design issue of a newly initiated study planned to assess directly the respiratory health impact of acid aerosols in North American children.

Six-Cities Study

As part of the Six-Cities Study we recognized the need to develop technology for measuring particulate and gaseous H^+ concentrations in the field setting. Samplers and analytic methods for aerosol strong acidity have been developed and are being used in the Six-Cities Study (11).

Preliminary data indicate that although sulfate levels were only slightly higher in Kingston-Harriman, 73.6 nmole/m^3, than in St. Louis, 61.6 nmole/m^3, during 1985–1986. The mean of H^+ ion concentrations actually determined was in fact higher in Kingston-Harriman, 36.1 nmole/m^3, than in St. Louis, 10.3 nmole/m^3 (Fig. 1). Spengler et al. describe results from four of the six cities (12).
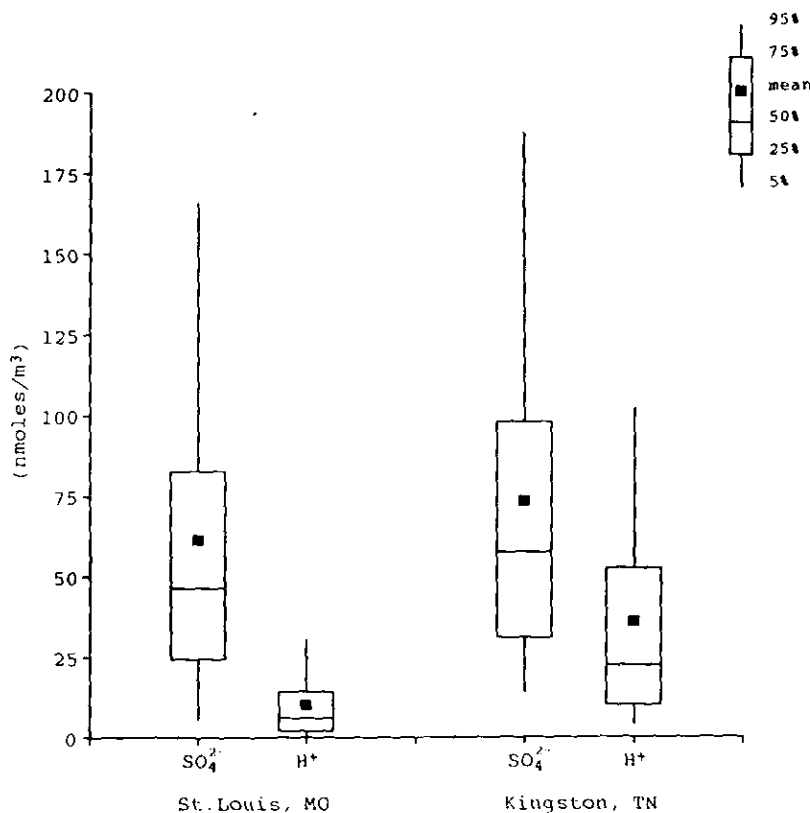

FIGURE 1. Distribution of sulfate (SO_4^{2-}) and hydrogen ion (H^+) concentration in St. Louis, MO, and Harriman, TN. Reprinted with permission (11).

In a recent presentation of results for the 1980–1981 school year for children aged 7 to 11 years old, we summarized the incidence of bronchitis in the previous year reported by parents (13). These results, adjusted for age, were graphed by city against the inhaled particulate (PM_{15}) average level measured over the 12 months prior to the time the child was seen (Fig. 2). It is noteworthy that the prevalence of reported bronchitis in Kingston is higher than would be expected given the level of PM_{15} (Fig. 2). In many comparisons between cities (13,14), Kingston has higher than expected frequencies of respiratory symptoms. Lippmann (15) has suggested that this excess may be due to higher aerosol acidity levels in Tennessee than in the other cities. In fact, mean H^+ concentrations presented earlier were higher in Kingston than any of the other three cities (12).

No direct aerosol acidity measurements were made during or before the 1980–1981 school year, when these children were examined. If these city-specific prevalences of bronchitis are replotted against mean H^+ concentrations for four cities presented earlier by Spengler (12), there is a relative shift in the ordering of the cities (Fig. 3), which suggests a better correlation of bronchitis prevalence with H^+ than with PM_{15}.

Currently in the Six-Cities Study, acid measurements are being made in each of the cities for a 1-year period. In conjunction with these measurements, daily respiratory symptoms of approximately 300 children in each city are being monitored using a diary technique supplemented by biweekly telephone contact (16). To date, data collection has been completed in five cities, and these data are currently being analyzed using
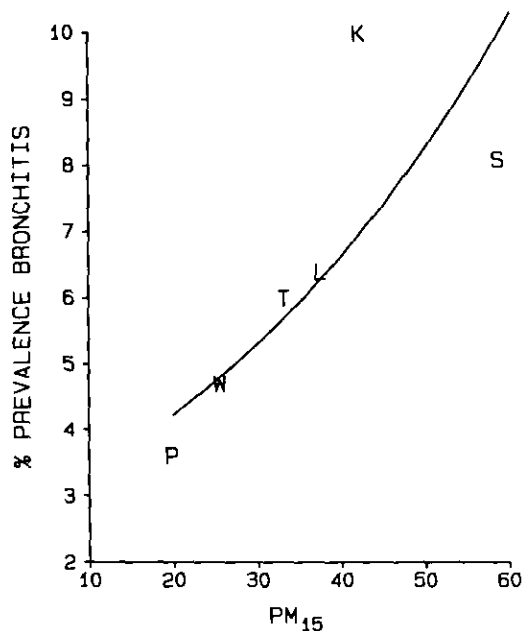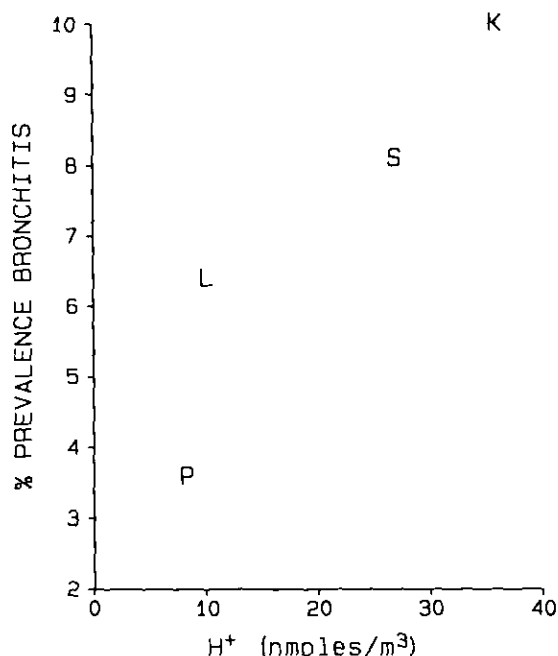

FIGURE 3. Bronchitis in the last year, children 10 to 12 years of age in four U.S. cities by hydrogen ion concentrations. See Fig. 2 for abbreviations.

Markov (17) and random effects (18) models of the serial observations. Such analyses should provide powerful data to assess the acute effects of acid aerosols on symptom frequency in these children.

Multi-City Acid Aerosol Study

To directly assess the chronic effects of acid aerosols on the respiratory health of children, we have proposed a multi-city study in collaboration with investigators from the Long Range Transport of Air Pollutants (LRTAP) Health Effects section of Health and Welfare, Canada. The study has just begun, and there are a number of design issues that are currently under review. One issue we would like to discuss relates to criteria for site selection.

The plan of our study is first to characterize exposure by collecting detailed acid aerosol measurements along with measurements of SO_2, NO_2, and ozone (O_3) for a 1-year period prior to carrying out a health survey on children aged 7 to 11 in the area. The aerometric measures will be based on 24-hr recordings taken every other day for a full year, with particular care in obtaining 12-hr samples over the summer months when acid events are predicted to be more frequent. These measures will then be used as surrogates for estimating chronic exposure defined as both level and frequency of excursions over specific defined acid aerosol levels for the lives of the children in the study.

After a 1-year period of collection of environmental data, children from the chosen communities, selected by school districts, will be visited in their schools. The

FIGURE 2. Bronchitis in the last year, children 10 to 12 years of age in six U.S. cities, by PM_{15}. P = Portage, WI; T = Topeka, KS; W = Watertown, MA; K = Kingston, TN; L = St. Louis, MO; S = Steubenville, OH.

project will be explained to them and they will be asked to take home a questionnaire to their parents to provide information about the home environment, the child's past medical history, current symptomatology, demography of the household, and smoking habits and disease frequency of the parents. Much of this information has been gathered for several years in a standardized fashion using the Six-Cities Study modification of the ATS/DLD children's questionnaire (19). Finally, the parent will be asked to sign a permission slip allowing us to examine the child in school.

Upon return of the completed questionnaire to the school and review for completion by our staff, a scheduled visit to the school will be made by our field team. At this visit each child will undergo spirometry in a standardized manner. While seated in a comfortable chair, with noseclip in place, the child will breath tidally on a dry rolling seal spirometer (Morgan Company, Andover, MA). At the end of a normal inspiration, the child will be asked to breath out as hard and fast as he/she can to residual volume (RV). This will be followed by a maximal inspiration to total lung capacity followed by another forced expiratory maneuver to RV. Both the partial and the entire flow volume curve will be recorded. The procedure will be repeated to obtain three acceptable tracings using ATS standard criteria (19). All volumes will be converted to body temperature and pressure, saturated (BTPS). The child's height and weight in stocking feet will be measured.

These forced partial and maximal expiratory maneuvers will be used to derive a series of measures on each child that characterize the pulmonary function status of the child in terms of normal growth, airway size, and, potentially, airway tone. To the degree that the information gathered from the parent can be used to adjust for potential confounding or risk modifying factors, the difference seen between children from different communities can be associated with differences in levels of exposure to ambient levels of acid aerosol exposures.

How we get from the data collection to this last test of association is not so trivial and is worth spending some time discussing. The basic design of the study was suggested to us by Professor John Tukey, who was one of our advisors on the Six-Cities Study. In that study, we were faced in all of our regression analyses with the phenomenon that our point estimates for each city were quite good, with each estimate usually based on more than 1000 observations. However, when we combined the data across six communities and tried to use the exposure data in a continuous manner, our true sample size often fell to something more like 6 rather than 6000. Thus, all of our cross-sectional analyses in the Six-Cities Study that try to assess the effect of the ambient exposure gradient across the six communities suffer from a lack of statistical power. Only because the study has been longitudinal, with repeated measures on the same children, and the fact

that exposure levels have been changing can we make definitive statements about the results. We have taken this phenomenon into account in the design of the new study.

The new study can be considered prospective from the perspective that the aerometric measures (exposure) precede the measure of respiratory symptoms and pulmonary function (effects). However, in terms of formal design (and significantly affecting cost) the study must be considered as a prevalence cross-sectional study rather than an incidence (i.e., longitudinal) study. The subjects are to be seen at only one point in time. We are postulating that their cumulative life events will be manifest in their histories and pulmonary function levels at least for those that are lifelong residents of their individual communities. If we can control for those important known risk factors and can demonstrate a difference between children from communities with and without significant acid aerosol pollution, we may be able to conclude that these differences are associated with not only the levels found in the previous monitored year but also that the ambient measures recorded are likely to reflect what has been occurring over the 7- to 10-year life span of the children.

Our objective in studying groups of children is to maximize the differences in exposure levels to construct an exposure-response relationship and at the same time to minimize the variance of any single point estimate about the line that summarizes the exposure-effect relation. Data available from the Six-Cities Study were used to estimate the level of difference we might expect in symptom frequency among groups of exposed and unexposed children. With this information we calculated the sample size necessary to have sufficient power to have a chance of finding a difference if one was present. Given approximately an 8 to 15% occurrence of most symptoms in the unexposed groups, to detect a 40% increase in risk of any given symptom, with sample series of 600 children in each community, by studying 24 communities our power to detect such an increase in risk is between 0.74 and 0.92. This estimate also takes into account the expected between town variances.

Thus, our plan is to enter three sets of eight sites over 3 years into the study. In each site we anticipate seeing more than 700 children to have approximately 600 lifelong residents of the community in the study. In contrast to the 40% excess risk to be detected for symptoms, for pulmonary function measures similar calculations suggest that we should be able to detect approximately a 0.5 to 3.0% difference in lung function level. Given that the magnitude of the passive smoking effect in children is in the range of 1% for the age group we will be studying (20) and the fact that colleagues from Canada were able to detect a 2% difference in lung function level between two groups of five communities (21), we believe that the power to detect significant difference in lung function is both sufficient and potentially of biologic importance. Time does not

permit me to fully justify this statement here, and interested readers should see indicated references on the natural history of the development of chronic obstructive pulmonary disease (COPD) (22–24).

To maximize our chances to find significant differences between communities at different levels of exposure we must deal with the anticipated chemistry. From the few studies that have attempted to monitor acid, it is clear that at least two distinct sources can be identified. We know that downwind from urban areas with major transportation sources, significant levels of nitric oxides and acid may occur. In addition acid aerosols result from long-range transport of pollutants generated from the combustion of fossil fuels (SO_2 and particulates), which are converted in the atmosphere to sulfuric acid. To the degree that this might occur independently of NO_x downwind from metropolitan areas, it would appear to relate to the height to which the emissions are dispersed and to the distance in the atmosphere the air masses have traveled before affecting a distant region or being precipitated out as acid rain. In each case, at least in the summer because of reactions in the sunlight, these major classes of different acids may occur in conjunction with or separate from elevated levels of O_3. In winter, the pollutants most likely to accumulate in the atmosphere are the sulfur oxides. Recent studies have suggested that O_3 may act independently of acid components in the air to affect respiratory symptoms (25) and, at least acutely, level of pulmonary function (26). Thus, the problem in studying the chronic effects of acid aerosols is to identify sites in which differences in levels of exposures to ozone, sulfates, and nitrates can be found.

Thus, in selecting sites, we must identify three replicates that meet the criteria indicated in Table 1. This would provide the most efficient design and allow us to test each pollutant separately and in combination with each other. We need, therefore, to define what is meant by high and low for each pollutant. Table 2 is one of our preliminary attempts at doing this and points out the ranges that we believe can be studied.

The pollution level is only one criteria, albeit a critical one, in defining potential study sites. We also must consider the demography of the site. Table 3 summarizes the criteria that must be set for an area to be considered acceptable. We found that we would be forced to restrict on race to avoid the potential confounding of the interaction of city and race. Similarly,

Table 1. Replicates for site selection.

O_3	H_2SO_4	HNO_3
High	High	High
High	High	Low
Low	High	High
Low	High	Low
High	Low	High
High	Low	Low
Low	Low	High
Low	Low	Low

Table 2. Ranges of annual mean and maximum pollution levels for high/low classification of exposure.

Sampling period	O_3, ppb/hr	SO_4^{2-}, µg/m³/day	NO_3^-, µg/m³/day	H_2SO_4, µg/m³/day
High				
Maximum	> 100[a]	> 30	> 10	> 15
Mean	> 50[b]	> 12	> 5	> 3
Low				
Maximum	< 80[a]	< 20	< 3	< 10
Mean	< 30[b]	< 3	< 1	< 1

[a]1-hr maximum.
[b]7-hr mean (May–September).

Table 3. Demographic characteristics for communities to be included in Multi-City Acid Aerosol Study.

Population	At least 2000 white families with children under 18 years of age
Race	At least 85% of the total population should be white
Family income	No more than 5% of all families with children under 18 years of age should have a family income below the poverty level
Stability	At least 70% of the residents over 5 years of age should have lived in the same county for the past 5 years
Cooking fuel	The proportion of housing units using electricity as their cooking fuel should be between 15 and 85%

we wanted social class (with family income as a surrogate) to be relatively homogeneous and wanted to avoid a major difference in indoor sources (i.e., cooking fuels) as a potential confounder.

In an attempt to be in the field within the first 2 months of the study, we decided to select the first four sites, such that in addition to meeting the criteria defined previously, the sites would also be close to a monitoring site in the U.S. and Canadian acid rain network run jointly by the U.S. Environmental Protection Agency, the Electric Power Research Institute, the Canadian Atmospheric and Environment Service, and the Ontario Ministry of the Environment. These network sites have been established to evaluate models of acid rain deposition. These sites should all be operating beginning in the fall-winter of 1987. Table 4 identified these sites in the categories corresponding to our best estimates of what will be measured as to level of O_3, (H_2SO_4), or (HNO_3). From these selected sites field personnel will visit the area to determine suitability, and this large multidisciplinary effort will be underway.

For this effort to be successful will take not only a large effort by a committed and technically competent staff, but also a very significant degree of cooperation from local health departments and school boards, children, and their parents. We hope that if another workshop on acid aerosols is organized for 3 years from now, we will be able to return to present at least part of the results of this endeavour.

Table 4. Preliminary sites selected for Multi-City Study.

O_3	H^+ SO_2	H^+ NO_x	Experimental design categories of pollution characteristics
High	High	High	North Central/urban complex 20–80 km New York City suburbs Southwestern Connecticut Pittsburgh suburbs Southeastern Pennsylvania Central New Jersey Southern Ontario St. Louis suburbs Ohio Northern West Virginia Maryland Northern Virginia Delaware
High	High	Low	North Central/urban complex > 100 km Upstate New York Kentucky West Virginia Virginia Indiana Southern Illinois
Low	High	High	Northern/urban complex 20–80 km New England Northern Illinois Southern Michigan
Low	High	Low	Local sources—acid plants/smelters
High	Low	High	Southern/urban complex 20–80 km Southern Texas Southern Louisiana Mississippi Southern California
High	Low	Low	Southern/urban complex > 100 km Southern Florida Central California
Low	Low	High	Northern/urban complex 20–80 km Northern California Southern Oregon
Low	Low	Low	Baseline pollution level Northern Wisconsin Minnesota Montana North Dakota Manitoba Saskatchewan Western Ontario

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